A Comparison Study of Clinicopathologic Characteristics of Southern California Asian American Non-small Cell Lung Cancer (NSCLC) Patients by Smoking Status

Sai-Hong Ignatius Ou, MD, PhD,†‡ Argyrios Ziogas, PhD,†‡ and Jason A. Zell, DO, MPH*†‡*

Background: We previously reported that Asian ethnicity is a favorable prognostic factor for overall survival (OS) in non-small cell lung cancer (NSCLC) patients independent of smoking status. However, Asian ethnicity represents a diverse and heterogeneous population. In this report, we compared the clinicopathologic characteristics of Asian American NSCLC patient subgroups by smoking status.

Methods: Clinicopathologic characteristics of the five major Asian American NSCLC patient subgroups diagnosed between 1991 and 2005 from three Southern California counties were analyzed. Prognostic factors for OS were evaluated by Cox multivariate analysis.

Results: One thousand one hundred twenty-four NSCLC patients were analyzed: Filipino American (37.0%), Vietnamese American (32.8%), Japanese American (11.8%), Chinese American (11.7%), and Korean American (6.7%). A total of 25.7% of these patients were never smokers. With the exception of Japanese American, most of Asian American were native born. Median age of never smokers was marginally younger than ever smokers (66 years versus 68 years, respectively, $p = 0.0507$). The proportion of never smokers who were women was 72.7% and ranged from the lowest among Korean American women (66.7%) to the highest among Japanese American women (84.2%). Among female patients, Vietnamese American patients had the highest proportion of being never smokers (65.5%). Significantly more never smokers (60.9%) than ever smokers (47.9%) presented with stage 4 disease. There was no statistical significant difference in OS between never smokers and ever smokers (11 versus 10 months; $p = 0.3040$). Tumor-related factors (stage and histologic differentiation) and treatment (surgery and chemotherapy) were independent prognostic factors for survival.

Conclusions: We found no statistical significant difference in clinicopathologic features or survival outcome between individual Asian American subgroup when analyzed according to smoking status.

Key Words: Non-small cell lung cancer, Asian American, Filipino American, Vietnamese American, Chinese American, Japanese American, Korean American, Never smoker, California Cancer Registry, Prognostic factors.

(*J Thorac Oncol.* 2010;5: 158–168)

Although tobacco-related lung cancer mortality is the number 1 cause of cancer death globally, deaths from lung cancer patients who were never smokers accounts for the seventh most common cancer cause of death globally.[1] Lung cancer in never smokers is commonly adenocarcinoma histology, predominantly occurs in women, presents with advanced stage, harbors mutations in the epidermal growth factor receptor (EGFR) but not K-*ras*, and possesses different mutation profiles in the p53 tumor suppressor gene (transversions in smokers and transitions in never smokers).[2–4] Lung cancer in never smokers also responds better to chemotherapy and has better survival outcome.[5–7] There is a remarkable regional variation in the proportion of lung cancer patients who are never smokers. Never smokers with lung cancer are found in greater proportion among Asians, especially Asian women.[2,3] Lung cancer is the most common cancer cause of mortality for the five most populous Asian American subgroups (Chinese American, Vietnamese American, Filipino American, Japanese American, and Korean American) in the United States.[8] Lung cancer is also the most common cancer cause of mortality for the same five subgroups in California except for Vietnamese American women.[9] We have shown that Asian American ethnicity is an independent favorable prognostic factor after factoring in smoking status in a multivariate analysis among non-small cell lung cancer (NSCLC) patients in Southern California.[10] However, Asian Americans are extremely diverse with respect to country of origin, socioeconomic status (SES), time since immigration, language spoken, religion practiced, and many other characteristics that affect health outcome. Studies have shown that different Asian American subgroups in the United States have different cancer burdens, that individual Asian American subgroups should be monitored separately, and that presenting one statistical estimate for Asian Americans does not accurately depict cancer burden of any different Asian subgroup.[8,9] Further-

*Division of Hematology/Oncology, Department of Medicine, Chao Family Comprehensive Cancer Center, University of California Irvine Medical Center, Orange, California; †Genetic Epidemiology Research Institute; and ‡Department of Epidemiology, School of Medicine, University of California Irvine, Irvine, California.

Disclosure: The authors declare no conflicts of interest.

Address for correspondence: Sai-Hong Ignatius Ou, MD, PhD, Chao Family Comprehensive Cancer Center, University of California Irvine Medical Center, 101 The City Drive South, Bldg 56, Rm 241, RT 81, Orange, CA 92868-3298. E-mail: ignatius.ou@uci.edu

The ideas and opinions expressed herein are those of the author(s) and endorsement by the State of California, Department of Public Health the National Cancer Institute, and the Centers for Disease Control and Prevention or their contractors and subcontractors is not intended nor should be inferred.

ISSN: 1556-0864/10/0502-0158

more, although Asian American may have lower lung cancer risk when compared with whites, the lung cancer risk is different among different Asian American subgroups.[11]

In 2007, the U.S. census bureau estimated that California is home to 4.5 million Asian Americans (34% of the total Asian American population in the United States). In this report, we describe and compare clinicopathologic characteristics and survival outcomes of the five most common Asian American NSCLC patient subgroups (Filipino American, Vietnamese American, Japanese American, Chinese American, and Korean American) in three counties of Southern California.

PATIENTS AND METHODS

Population

This is a retrospective data analysis from the Cancer Surveillance Programs of Orange, San Diego, and Imperial counties in Southern California databases covering an area with estimated population of 6.0 million. The five most populous Asian American NSCLC patients in the three counties (Filipino Americans, Vietnamese Americans, Japanese Americans, Chinese Americans, and Korean Americans) who were diagnosed between 1991 and 2005 and had complete follow-up data up to December 2007 were included in the study. Tumor site was abstracted as previously described.[12] American Joint Committee on Cancer (AJCC) stage rather than Surveillance, Epidemiology, and End Results (SEER) summary stage (local, regional, or distant) was assigned to individual patients. For the period 1991–2002, AJCC stage was abstracted from existing AJCC codes and derived from SEER extent of disease codes where tumor, node, metastasis data were missing, as done previously.[10] For patients diagnosed between 2003 and 2005, SEER-AJCC summary staging was used. Demographic data including age, ethnicity, gender, marital status, surgery, radiation, and chemotherapy given during the first course of therapy were abstracted using SEER codes. Ethnicity data and marital status were obtained using California Cancer Registry (CCR) codes. Radiation therapy and surgical techniques were abstracted using SEER codes. Chemotherapy given during the first course of therapy was ascertained using CCR codes. The measurement of SES used in this analysis was a composite measure using CCR and census data as previously described.[12]

Smoking status was abstracted using a customized text mining program in SAS 9.2 (SAS Institute, Inc., Cary, NC) that examines text files of individual patient records as previously described.[10,13] Patients with any documented history of smoking were classified as "ever smokers." Patients with documentation of no smoking history were classified as "never smokers." Patients lacking documented information on smoking history were excluded from this analysis.

Statistical Analyses

Comparisons of demographic, clinical, and pathologic variables were made for NSCLC patients, using Pearson χ^2 statistic for nominal variables and Student t test for continuous variables. Univariate survival rate analyses were estimated using the Kaplan-Meier method, with comparisons made between groups by the log-rank test. Cox proportional hazards modeling using time since diagnosis were performed. All statistical analyses were conducted using SAS 9.2 statistical software (SAS Institute, Inc.). Statistical significance was assumed for a two-tailed p value less than 0.05.

Ethical Considerations

This research study was approved by the University of California Irvine Institutional Review Board (2007-6078).

RESULTS

Characteristic of Asian American NSCLC Patients

Between 1991 and 2005, a total of 1124 patients from Southern California were analyzed, comprising the five major Asian American NSCLC patient subgroups having complete follow-up data and known smoking status. Two hundred eighty-nine patients (25.7%) were never smokers. There were 575 patients with unknown smoking status were excluded from the analysis. The distribution of Asian American subgroups among those with unknown smoking status was similar to the distribution of Asian American subgroup with known smoking status reported in this study.

Period of Diagnosis

The proportion of Asian American NSCLC patients who were never smokers increased significantly with time: 16.5% (1991–1995), 25.7% (1996–2000), and 31.2% (2001–2005) ($p_{trend} < 0.0001$). Among female patients, the proportion of NSCLC patients who were never smokers also increased significantly (37.0%, 48.7%, and 59.5%, respectively, $p_{trend} = 0.0009$). The proportion of male NSCLC patients who were never smokers also increased, but the trend was not significant (9.1%, 11.7%, and 11.9%, respectively, $p_{trend} = 0.3598$). The proportion of never smokers within individual Asian American subgroup by period of diagnosis were plotted in Figures 1*A* (all patients), *B* (male), and *C* (female). Among individual Asian American subgroup, the trend of increasing proportion of never smokers was significant for Vietnamese American patients as a whole (16.7%, 22.8%, and 39.7%, respectively, $p_{trend} < 0.0001$) and for female Vietnamese American patients (40.0%, 46.3%, and 89.1%, respectively, $p_{trend} < 0.0001$). On the other hand, the proportion of female Filipino American NSCLC patients who were never smokers remained constant throughout the three periods of diagnosis (52.6%, 56.4%, and 54.1%, respectively, $p_{trend} = 0.9956$).

Age at Diagnosis

The median age of diagnosis of never smokers (66 years) was lower than that of ever smokers (68 years), and the difference was borderline significant ($p = 0.0507$) (Table 1). Female never smokers were significantly younger than female ever smokers (65 versus 69 years, $p = 0.0111$) (Table 1).

Histology

Significantly, more never smokers were diagnosed with adenocarcinoma (59.2%) than ever smokers (41.8%). Similarly, the proportion of bronchioloalveolar carcinoma diagnosed in never smokers was 8.7% compared with 3.4% in ever smokers. The proportion of squamous cell carcinoma

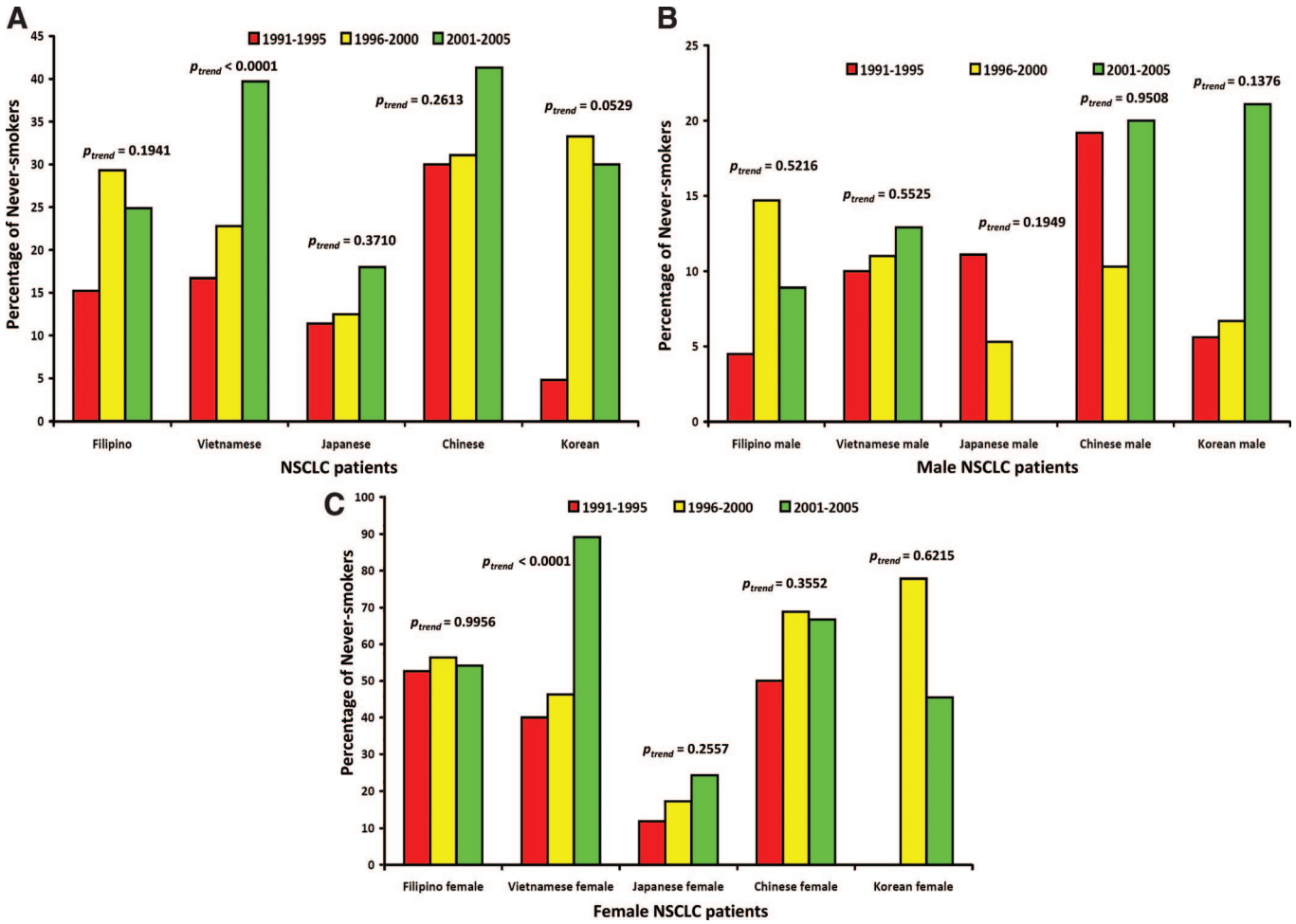

FIGURE 1. *A,* The proportion of never smokers among individual Asian American non-small cell lung cancer (NSCLC) patients by three periods of diagnosis. *B,* The proportion of male never smokers among individual Asian American NSCLC patients by three periods of diagnosis. *C,* The proportion of female never smokers among individual Asian American NSCLC patients by three periods of diagnosis.

was 24.7% in ever smokers to 7.3% in never smokers (Table 1).

Stage at Presentation

Significantly more never smokers (60.9%) presented with stage 4 NSCLC compared with ever smokers (47.9%, $p < 0.0001$), and the difference was similar for male ($p = 0.0014$) and female ($p = 0.0015$) patients (Table 1).

Asian American Subgroups

Filipino American (37.0%), Vietnamese American (32.8%), Japanese American (11.8%), Chinese American (11.7%), and Korean American (6.7%) constituted the Asian American NSCLC patient subgroups. The proportion of never smokers within individual Asian American subgroup was 34.3% (Chinese American), 28.5% (Vietnamese American), 24.5% (Filipino American), 24.0% (Korean American), and 14.3% (Japanese American) (Table 2). The median ages of diagnosis of never smokers and ever smokers among all five Asian American subgroups as a whole and by gender were listed in Table 2.

Gender

There were more male than female NSCLC patients within each Asian American subgroup except for Japanese Americans where 62.4% of patients were women (Table 3). Female patients comprised the majority of Asian American NSCLC never smokers and ranged from 66.7% among Korean American never smokers to 84.2% among Japanese American never smokers (Table 3). Among female patients, the proportion of female NSCLC patients who were never smokers ranged from the lowest (19.3%) among female Japanese American patients to the highest (65.5%) among female Vietnamese American patients (Table 2).

Socioeconomic Status

There was no statistical significant difference in the distribution of SES between never smokers and ever smokers as a whole (Table 1) or within each of the five Asian subgroups by smoking status (Table 3).

TABLE 1. Clinicopathologic Characteristics of Asian American NSCLC Patients by Smoking Status and Gender

	Total			Male			Female		
	Ever Smoker	**Never Smoker**	***p***	**Ever Smoker**	**Never Smoker**	***p***	**Ever Smoker**	**Never Smoker**	***p***
N (%)[a]	835 (74.3)	289 (25.7)		637 (89.0)	79 (11.0)		198 (48.5)	210 (51.5)	
Median age, yr (95% CI)	68 (47–83)	66 (44–86)	0.0507[b]	68 (47–82)	70 (38–89)	0.4306[b]	69 (47–85)	65 (44–85)	0.0111[b]
Median follow-up time, mo (95% CI)	9 (1–87)	10 (0–71)	0.5994[b]	8 (0–97)	7 (0–86)	0.3128[b]	10 (0–65)	11 (1–71)	0.6030[b]
Period of diagnosis			<0.0001			0.5736			0.0035
1991–1995	227 (27.2)	45 (15.6)		181 (28.4)	18 (22.8)		46 (23.2)	27 (12.9)	
1996–2000	295 (35.3)	102 (35.3)		218 (34.2)	29 (36.7)		77 (38.9)	73 (34.8)	
2001–2005	313 (37.5)	142 (49.1)		238 (37.4)	32 (40.5)		75 (37.9)	110 (52.4)	
Age, yr			0.0280			0.0007			0.0280
0–39	5 (2.5)	8 (2.8)		5 (0.8)	4 (5.1)		5 (2.5)	8 (3.8)	
40–49	8 (4.0)	21 (10.0)		43 (6.8)	6 (7.6)		8 (4.0)	21 (10.0)	
50–59	40 (20.2)	48 (22.9)		103 (16.2)	8 (10.1)		40 (20.2)	48 (22.9)	
60–69	47 (23.7)	55 (26.2)		199 (31.2)	20 (25.3)		47 (23.7)	55 (26.2)	
70–79	73 (36.9)	49 (23.3)		228 (935.8)	25 (31.7)		73 (36.9)	49 (23.30)	
80+	25 (12.6)	29 (13.8)		59 (9.3)	16 (20.3)		25 (12.6)	29 (13.8)	
Sex			<0.0001						
Male	637 (76.3)	79 (27.3)		—	—		—	—	
Female	198 (23.7)	210 (72.7)		—	—	—	—	—	—
Asian American subgroup			0.0029			0.4202			<0.0001
Filipino American	314 (37.6)	102 (35.3)		253 (39.70)	28 (35.4)		61 (30.8)	74 (35.2)	
Vietnamese American	264 (31.6)	105 (36.3)		224 (35.2)	29 (36.7)		40 (20.2)	76 (36.2)	
Japanese American	114 (13.7)	19 (6.6)		47 (7.4)	3 (3.8)		67 (33.8)	16 (7.6)	
Chinese American	86 (10.3)	45 (15.6)		67 (10.50)	13 (16.5)		19 (9.6)	32 (15.2)	
Korean American	57 (6.8)	18 (6.2)		46 (7.2)	6 (7.6)		11 (5.6)	12 (5.7)	
Histology			<0.0001			0.0025			<0.0001
Adenocarcinoma	349 (41.8)	171 (59.2)		260 (40.8)	48 (60.8)		89 (45.0)	123 (58.6)	
BAC	28 (3.4)	25 (8.7)		20 (3.1)	2 (2.5)		8 (4.0)	23 (11.0)	
Large cell	50 (6.0)	16 (5.5)		40 (6.3)	8 (10.1)		10 (5.1)	8 (3.8)	
Squamous cell	206 (24.7)	21 (7.3)		162 (25.4)	9 (11.4)		44 (2.2)	12 (5.7)	
Mixed/NOS/other	202 (24.2)	56 (19.4)		155 (24.3)	12 (15.2)		47 (23.7)	44 (21.0)	
Histologic differentiation			0.0012			0.6917			0.0055
Well	28 (3.4)	18 (6.2)		22 (3.5)	1 (1.3)		6 (93.0)	17 (8.1)	
Moderately	117 (14.0)	48 (16.6)		83 (13.0)	11 (13.9)		34 (17.2)	37 (17.6)	
Poorly	285 (34.1)	76 (26.3)		221 (34.7)	29 (36.7)		64 (32.3)	47 (22.4)	
Undifferentiated	42 (5.0)	4 (1.4)		33 (5.2)	2 (2.5)		9 (4.6)	2 (1.0)	
Unknown	363 (43.5)	143 (49.5)		178 (43.6)	36 (45.6)		85 (42.9)	107 (51.0)	
AJCC stage			0.0004			0.0014			0.0015
Stage 1	80 (9.6)	30 (10.4)		63 (9.9)	5 (6.3)		17 (8.60)	25 (11.9)	
Stage 2	38 (4.6)	4 (1.4)		29 (4.6)	2 (2.5)		9 (4.6)	2 (1.0)	
Stage 3	194 (23.2)	44 (15.2)		136 (21.4)	9 (11.4)		58 (29.30)	35 (16.7)	
Stage 4	400 (47.9)	176 (60.9)		318 (49.9)	59 (74.7)		82 (41.4)	117 (55.7)	
Unknown	123 (14.7)	35 (12.1)		91 (14.3)	4 (5.1)		32 (16.2)	31 (14.8)	
Socioeconomic status			0.4874			0.3520			0.6875
SES1 (lowest)	96 (11.5)	30 (10.4)		79 (12.4)	6 (7.6)		17 (8.6)	24 (11.4)	
SES2	177 (21.2)	56 (19.4)		133 (20.9)	12 (15.2)		44 (22.2)	44 (21.0)	
SES3	215 (25.7)	65 (22.5)		170 (26.7)	20 (25.3)		45 (22.7)	45 (21.4)	
SES4	187 (22.4)	68 (23.5)		137 (21.5)	23 (29.1)		50 (25.3)	45 (21.4)	
SES5 (highest)	146 (17.5)	62 (21.5)		108 (17.0)	14 (17.7)		38 (19.2)	48 (22.9)	
Unknown	14 (1.7)	8 (2.8)		10 (1.6)	4 (5.1)		4 (2.0)	4 (1.9)	
Marital status			0.1208			0.9974			0.0136
Married	609 (72.9)	194 (67.1)		515 (80.6)	64 (81.0)		94 (47.5)	130 (61.9)	
Unmarried	203 (24.3)	88 (30.5)		105 (16.5)	13 (16.5)		98 (49.5)	75 (35.7)	
Unknown	23 (2.8)	7 (2.4)		17 (2.7)	2 (92.5)		6 (3.0)	5 (2.4)	

(*Continued*)

TABLE 1. (*Continued*)

	Total			Male			Female		
	Ever Smoker	Never Smoker	*p*	Ever Smoker	Never Smoker	*p*	Ever Smoker	Never Smoker	*p*
Surgery			0.8695			0.4018			0.8781
Yes	183 (21.9)	62 (21.5)		139 (21.8)	14 (17.7)		44 (22.2)	48 (22.9)	
No	652 (78.1)	227 (78.6)		498 (78.2)	65 (82.3)		154 (77.8)	162 (77.1)	
Radiation			0.0067			0.2444			0.1371
Yes	377 (45.2)	104 (36.0)		294 (46.2)	31 (39.2)		83 (41.9)	73 (34.8)	
No	458 (54.8)	185 (64.0)		343 (53.9)	48 (60.8)		115 (58.1)	137 (65.2)	
Chemotherapy			0.1170			0.1899			0.4685
Yes	310 (37.1)	125 (43.3)		234 (36.7)	37 (46.8)		76 (38.4)	88 (41.9)	
No	522 (62.5)	164 (56.8)		400 (62.8)	42 (53.2)		122 (61.6)	122 (58.1)	
Unknown	3 (0.4)	0 (0.0)		3 (0.5)	0 (0.0)		0 (0.0)	0 (0.0)	

[a] Percentage calculated across the row.
[b] *p* value calculated by Wilson two-sample test.
NSCLC, non-small cell lung cancer; BAC, bronchoalveolar carcinoma; AJCC, American Joint Committee on Cancer; SES, socioeconomic status; NOS, not otherwise specified.

TABLE 2. Median Age of Diagnosis of Individual Asian American Subgroup

Smoking Status	Never Smoker	Ever Smoker	*p*	Never Smoker	Ever Smoker	*p*	Never Smoker	Ever Smoker	*p*
	All (*N* = 416)			**Male (*N* = 281)**			**Female (*N* = 135)**		
Filipino American			0.2557			0.4176			0.4019
N (%)	102 (24.5)	314 (75.5)		28 (10.0)	253 (90.0)		74 (54.8)	61 (45.2)	
Median age (95% CI)	67 (43–5)	68 (45–84)		70 (38–89)	69 (48–83)		65 (43–85)	67 (42–85)	
	All (*N* = 369)			**Male (*N* = 253)**			**Female (*N* = 116)**		
Vietnamese American			0.6600			0.3625			0.1415
N (%)	105 (28.5)	264 (71.5)		29 (11.5)	224 (88.5)		76 (65.5)	40 (34.5)	
Median age (95% CI)	65 (41–86)	67 (45–83)		68 (38–89)	66 (45–82)		64 (44–86)	70 (38–89)	0.1415
	All (*N* = 133)			**Male (*N* = 50)**			**Female (*N* = 83)**		
Japanese American			0.6294			0.5261			0.5364
N (%)	19 (14.3)	114 (85.7)		3 (6.0)	47 (84.0)		16 (19.3)	67 (80.7)	
Median age (95% CI)	66 (49–82)	609 (51–83)		74 (71–81)	73 (48–83)		65 (49–82)	67 (54–83)	
	All (*N* = 131)			**Male (*N* = 80)**			**Female (*N* = 51)**		
Chinese American			0.0639			0.5745			0.0141
N (%)	45 (34.4)	86 (65.6)		13 (16.2)	67 (83.8)		32 (62.7)	19 (37.3)	
Median age (95% CI)	69 (45–85)	73 (52–83)		69 (45–90)	72 (52–82)		68 (44–85)	76 (52–90)	
	All (*N* = 75)			**Male (*N* = 52)**			**Female (*N* = 23)**		
Korean American			0.4197			0.4474			1.000
N (%)	18 (24.0)	57 (76.0)		6 (11.5)	46 (88.5)		12 (52.2)	11 (47.8)	
Median age (95% CI)	57 (39–87)	65 (48–81)		59 (49–86)	63 (48–81)		56 (39–87)	69 (49–76)	

Place of Origin

Most of Filipino American (86.1%), Vietnamese American (83.7%), Korean American (72.0%), and Chinese American (70.2%) NSCLC patients were born in their native countries whereas slightly less than half of Japanese American patients were native born (48.1%). However, most Japanese American never smokers (57.9%) were still born in Japan (Table 4). Furthermore, the proportion of Japanese never smokers was higher among native Japanese (17.2%) than nonnative Japanese (11.6%) NSCLC patients (Table 5).

Univariate Survival Analysis

Period of Diagnosis

The median overall survival (OS) improved over time: 9 months (1991–1995), 10 months (1996–2000), and 12 months (2001–2005), and the difference was borderline statistically significant ($p = 0.0524$).

TABLE 3. Clinicopathologic Characteristics of Individual Asian American Subgroup by Smoking Status

	Filipino American			Vietnamese American			Chinese American			Japanese American			Korean American		
	Ever Smoker	Never Smoker	*p*	Ever Smoker	Never Smoker	*p*	Ever Smoker	Never Smoker	*p*	Ever Smoker	Never Smoker	*p*	Ever Smoker	Never Smoker	*p*
N (%)[a]	314 (75.5)	102 (24.5)		264 (71.5)	105 (28.5)		86 (65.7)	45 (34.3)		114 (85.7)	19 (14.3)		57 (76.0)	18 (24.0)	
Gender			<0.0001			<0.0001			<0.0001			0.0341			0.0001
Male	253 (80.6)	28 (27.5)		224 (84.9)	29 (27.6)		67 (77.9)	13 (28.9)		47 (41.2)	3 (15.8)		46 (80.7)	6 (33.3)	
Female	61 (19.4)	74 (72.5)		40 (15.1)	76 (72.4)		19 (22.1)	32 (71.1)		67 (58.8)	16 (84.2)		11 (19.3)	12 (66.7)	
Age category, yr			0.2624			0.2260			0.0067			0.9129			0.0300
0–9	5 (1.6)	5 (4.9)		5 (1.9)	5 (4.8)		0 (0.0)	1 (2.2)		0 (0.0)	0 (0.0)		0 (0.0)	1 (5.6)	
40–9	18 (5.7)	7 (6.9)		23 (8.7)	11 (10.5)		2 (2.3)	6 (13.3)		4 (3.5)	1 (5.3)		4 (7.0)	2 (11.1)	
50–9	56 (17.8)	16 (15.7)		49 (18.6)	19 (18.1)		9 (10.5)	10 (22.2)		18 (15.8)	4 (21.1)		11 (19.3)	7 (38.9)	
60–9	89 (28.3)	32 (31.4)		79 (29.9)	29 (27.6)		19 (22.1)	7 (15.6)		36 (31.6)	5 (26.)		23 (40.4)	2 (11.1)	
70–0	116 (36.9)	29 (28.4)		84 (31.8)	25 (23.8)		44 (51.2)	12 (26.7)		43 (37.7)	6 (31.6)		14 (24.6)	2 (11.1)	
80+	30 (9.6)	13 (12.8)		24 (9.1)	16 (15.2)		12 (14.0)	9 (20.0)		13 (11.4)	3 (15.8)		5 (8.8)	4 (22.2)	
Histology			0.0024			0.0032			0.0215			0.0002			0.001
Adenocarcinoma	144 (45.9)	57 (55.9)		112 (42.4)	60 (57.1)		33 (38.4)	31 (68.9)		44 (38.6)	11 (57.9)		16 (28.1)	12 (66.7)	
BAC	13 (4.1)	12 (11.8)		9 (3.4)	7 (6.7)		4 (4.7)	2 (4.4)		2 (1.8)	4 (21.1)		0 (0.0)	0 (0.0)	
Large cell carcinoma	21 (6.7)	4 (3.9)		13 (4.9)	6 (5.7)		11 (12.8)	3 (6.7)		4 (3.5)	1 (5.3)		1 (1.8)	2 (11.1)	
Squamous cell carcinoma	75 (23.9)	11 (10.8)		54 (20.5)	6 (5.7)		16 (18.6)	4 (8.9)		38 (33.3)	0 (0.0)		23 (40.4)	0 (0.0)	
Undifferentiated	61 (19.4)	18 (17.7)		76 (28.8)	26 (24.8)		22 (25.6)	5 (11.1)		26 (22.8)	3 (15.8)		17 (29.8)	4 (22.2)	
AJCC stage			0.0857			0.3493			0.1141			0.6973			0.2462
Stage 1	27 (8.6)	11 (10.8)		26 (9.9)	11 (10.5)		7 (8.1)	3 (6.7)		16 (14.0)	3 (15.8)		4 (70)	2 (11.1)	
Stage 2	8 (2.6)	2 (2.0)		8 (3.0)	1 (1.0)		9 (10.5)	0 (0.0)		7 (6.1)	1 (5.3)		6 (1015)	0 (0.0)	
Stage 3	82 (26.1)	13 (12.8)		58 (22.0)	18 (17.1)		18 (20.9)	8 (17.8)		29 (25.4)	3 (15.8)		7 (12.3)	2 (11.1)	
Stage 4	156 (49.7)	60 (58.8)		137 (51.9)	65 (61.9)		37 (43.0)	28 (62.2)		42 (36.8)	10 (52.6)		28 (49.1)	13 (72.2)	
Unknown	41 (13.1)	16 (15.7)		35 (13.3)	10 (9.5)		15 (17.4)	6 (13.3)		20 (17.5)	2 (10.5)		12 (21.1)	1 (5.6)	
Histologic differentiation			0.0140			0.7563			0.5595			0.0305			0.7685
Well	8 (2.6)	8 (7.8)		6 (2.3)	3 (2.9)		6 (7.0)	3 (6.7)		4 (3.5)	3 (15.8)		4 (7.0)	1 (5.6)	
Moderately	38 (12.1)	18 (17.7)		42 (15.9)	15 (14.3)		10 (11.6)	8 (17.8)		17 (14.9)	4 (21.1)		10 (17.5)	3 (16.7)	
Poorly	119 (37.9)	30 (29.4)		71 (26.9)	24 (22.9)		27 (31.4)	14 (31.1)		44 (38.6)	2 (10.5)		24 (42.1)	6 (33.3)	
Undifferentiated	17 (5.4)	1 (1.0)		9 (3.4)	2 (1.9)		8 (9.3)	1 (2.2)		6 (5.3)	0 (0.0)		2 (3.5)	0 (0.0)	
Unknown	132 (42.0)	45 (44.1)		136 (51.5)	61 (58.1)		35 (40.7)	19 (42.2)		43 (37.7)	10 (52.6)		17 (29.8)	8 (44.4)	
Socioeconomic status			0.9832			0.2899			0.7666			0.6911			0.8672
SES1	44 (14.0)	12 (11.8)		41 (15.5)	16 (15.2)		5 (5.8)	1 (2.2)		4 (3.5)	1 (5.3)		2 (3.5)	0 (0.0)	
SES2	56 (17.8)	19 (18.6)		80 (30.3)	27 (25.7)		8 (9.3)	3 (6.7)		18 (15.8)	2 (10.5)		15 (26.3)	5 (27.8)	
SES3	89 (28.3)	28 (28.3)		73 (27.7)	22 (21.0)		19 (22.1)	8 (17.8)		26 (22.8)	5 (26.3)		8 (14.0)	2 (11.8)	
SES4	76 (24.2)	26 (26.3)		42 (15.9)	24 (22.9)		16 (18.6)	9 (20.0)		34 (29.8)	3 (15.8)		19 (33.3)	6 (33.3)	
SES5	45 (14.3)	14 (14.1)		27 (10.2)	15 (14.4)		35 (40.7)	22 (48.9)		31 (27.2)	7 (36.8)		8 (14.0)	4 (22.2)	
Unknown	4 (1.3)	3 (2.9)		1 (0.4)	1 (1.0)		3 (3.5)	2 (4.4)		1 (0.9)	1 (5.3)		5 (8.8)	1 (5.6)	

(*Continued*)

TABLE 3. (*Continued*)

	Filipino American			Vietnamese American			Chinese American			Japanese American			Korean American		
	Ever Smoker	Never Smoker	*p*	Ever Smoker	Never Smoker	*p*	Ever Smoker	Never Smoker	*p*	Ever Smoker	Never Smoker	*p*	Ever Smoker	Never Smoker	*p*
Marital status			0.3492			0.5526			0.4029			0.0590			0.8202
Married	241 (76.8)	72 (70.6)		186 (70.5)	69 (65.7)		55 (64.0)	28 (62.2)		76 (66.7)	9 (47.4)		51 (89.5)	16 (88.9)	
Unmarried	68 (21.7)	29 (28.4)		66 (25.0)	32 (30.5)		28 (32.6)	17 (37.8)		36 (31.6)	8 (42.1)		5 (8.7)	2 (11.1)	
Unknown	5 (1.6)	1 (1.0)		12 (4.5)	4 (3.8)		3 (2.5)	0 (0.0)		2 (1.8)	2 (10.5)		1 (1.8)	0 (0.0)	
Surgery			0.7434			0.6649			0.9865			0.5162			0.5312
Yes	66 (21.0)	23 (22.5)		53 (20.1)	19 (18.1)		19 (22.1)	10 (22.2)		28 (24.6)	6 (31.6)		17 (29.8)	4 (22.2)	
No	248 (79.0)	79 (77.5)		211 (9.9)	86 (81.9)		67 (77.9)	35 (77.8)		86 (75.4)	13 (68.4)		40 (70.2)	14 (77.8)	
Radiation			0.0030			0.1948			0.1010			0.1034			0.4045
Yes	148 (47.1)	31 (30.4)		115 (43.6)	38 (36.2)		33 (38.4)	24 (53.3)		59 (51.8)	6 (31.6)		22 (38.6)	5 (27.8)	
No	166 (52.9)	71 (69.6)		149 (56.4)	67 (63.8)		53 (61.6)	21 (46.7)		55 (48.2)	13 (68.4)		35 (61.4)	13 (72.2)	
Chemotherapy			0.8496			0.1783			0.0007			0.8318			0.9121
Yes	120 (38.2)	39 (38.2)		91 (34.5)	46 (43.8)		19 (22.1)	23 (51.1)		57 (50.0)	10 (52.6)		23 (40.4)	7 (38.9)	
No	193 (61.5)	63 (61.8)		171 (64.8)	59 (56.2)		67 (77.9)	22 (48.9)		57 (50.0)	9 (47.4)		34 (59.7)	11 (61.1)	
Unknown	1 (0.3)	0 (0.0)		2 (0.8)	0 (0.0)		0 (0.0)	0 (0.0)		0 (0.0)	0 (0.0)		0 (0.0)	0 (0.0)	

[a] Percentage calculated across row.
BAC, bronchoalveolar carcinoma; AJCC, American Joint Committee on Cancer; SES, socioeconomic status.

TABLE 4. Place of Origin of the Individual Asian American Subgroup

	Filipino American			Vietnamese American			Chinese American			Japanese American			Korean American		
	All	Never Smoker	Ever Smoker	All	Never Smoker	Ever Smoker	All	Never Smoker	Ever Smoker	All	Never Smoker	Ever Smoker	All	Never Smoker	Ever Smoker
N	416	102	314	369	105	264	131	45	86	133	19	114	75	18	57
Native born															
Yes (%)	358 (86.1)	90 (88.2)	268 (85.4)	309 (83.7)	92 (87.6)	217 (82.2)	92 (70.2)	33 (73.3)	59 (68.6)	64 (48.1)	11 (57.9)	53 (46.5)	54 (72.0)	12 (66.7)	42 (73.7)
No (%)	58 (13.9)	12 (11.8)	46 (14.6)	60 (16.3)	13 (12.4)	47 (17.8)	39 (29.8)	12 (26.7)	27 (31.4)	69 (51.9)	8 (42.1)	61 (53.5)	21 (28.0)	6 (33.3)	15 (26.3)

TABLE 5. Comparison of Native Versus Nonnative Japanese American NSCLC Patients

	Ever Smoker (%)[a]	Never Smoker (%)[a]
Native[b]		
All (N = 64)	53 (82.8)	11 (17.2)
Male (N = 11)	11 (100.0)	0 (0.0)
Female (N = 53)	42 (79.3)	11 (20.8)
Nonnative[b]		
All (N = 69)	61 (88.4)	8 (11.6)
Male (N = 39)	36 (92.3)	3 (7.7)
Female (N = 30)	25 (83.3)	5 (16.7)

[a] Percentage calculated across the row.
[b] Native, born in Japan; nonnative, not born in Japan.

Gender

Among never smokers, female patients had statistically significant improved OS compared with male patients (12 months versus 7 months; $p = 0.0258$). Among ever smokers, OS differences between female patients (11 months) and male patients (9 months) were not statistically significant ($p = 0.6621$).

Smoking Status

No statistically significant differences were observed between never smokers (11 months) and ever smokers (10 months) ($p = 0.3040$). Within individual Asian American subgroup, the median OS of Filipino American never smokers and ever smokers were 10 months and 9 months, respectively ($p = 0.7004$). For Vietnamese American, the corresponding median OS for never smokers and ever smokers were10 months and 7 months, respectively ($p = 0.3180$); for Japanese American, the corresponding median OS for never smokers and ever smokers were 16 months and 12 months, respectively ($p = 0.7352$); for Chinese American, the corresponding median OS were 12 months and 10 months, respectively ($p = 0.3446$); and finally, the corresponding median OS for Korean American never smokers and ever smokers were 12 months and 13 months, respectively ($p = 0.5817$).

Ethnicity

There was no statistically significant difference in OS among the five Asian American subgroups overall ($p = 0.1258$), among ever smokers ($p = 0.1131$), and among never smokers ($p = 0.8663$).

Chemotherapy

For stage 4 NSCLC patients, chemotherapy significantly improved OS for both ever smokers (8 months with chemotherapy versus 3 months without chemotherapy; $p < 0.0001$) and never smokers (11 months versus 3 months, respectively; $p = 0.0036$) (Figures 2*A*, *B*).

Multivariate Survival Analysis

We performed Cox proportional hazards analysis to identify potential independent prognostic factors. Cox proportional hazards analysis identified early AJCC stage, well-differentiated tumor, surgery (versus no surgery, hazard ratio = 0.0342, 95% confidence interval: 0.270–0.432; $p < 0.001$), and chemotherapy (versus no chemotherapy, hazard ratio = 0.595, 95% confidence interval: 0.511–0.692; $p < 0.0001$) were favorable independent prognostic factors after accounting for age, gender, smoking status, Asian American subgroup, histology, period of diagnosis, SES, marital status, and radiation (Table 6).

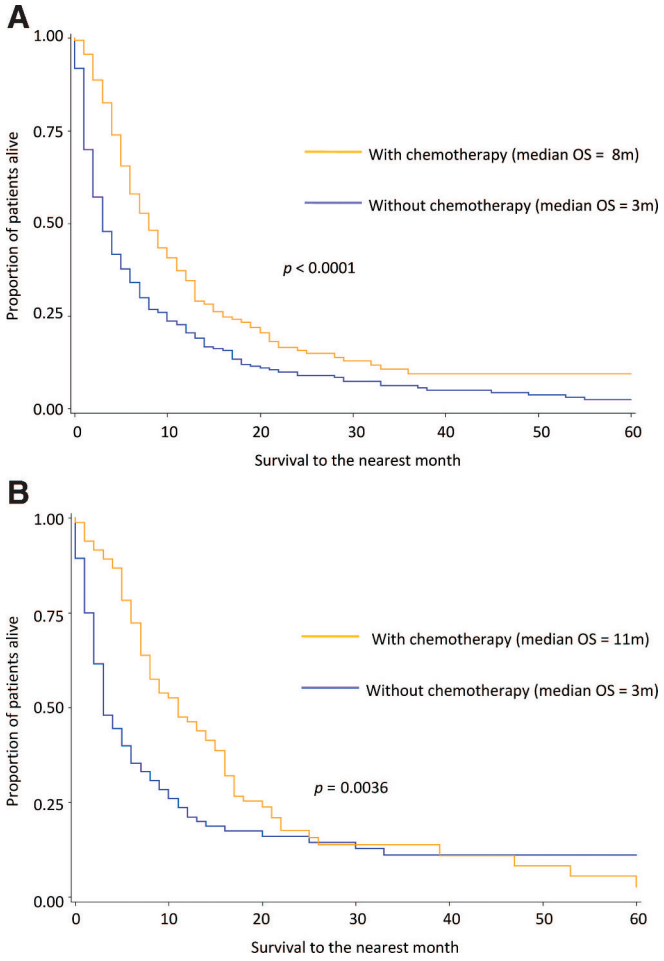

FIGURE 2. *A*, Kaplan-Meier survival curves of stage 4 ever smokers with or without chemotherapy. *B*, Kaplan-Meier survival curves of stage 4 never smokers with or without chemotherapy.

DISCUSSION

In this report, we provided further analysis of the clinicopathologic characteristics for the five major Asian American subgroups that constitute the majority of Asians in our study, which demonstrated that Asian ethnicity is an independent favorable prognostic factor for OS in NSCLC.[10] Clinicopathologic characteristics common to NSCLC patients who are never smokers were observed among all Asian American never smokers subgroups (younger age, predominance of female gender, adenocarcinoma and bronchioloalveolar carcinoma histologies, and advanced disease).

TABLE 6. Cox Proportional Hazards Model for OS

	OS	
	HR (95% CI)	***p***
Smoking status		0.5285
Ever smoker	1.000	
Never smoker	0.943 (0.787–1.131)	
Gender		0.7666
Male	1.000	
Female	0.975 (0.823–1.154)	
AJCC stage[a]		
1	1.000	
2	2.160 (1.385–3.368)	0.0007
3	2.177 (1.574–3.010)	<0.0001
4	3.527 (2.599–4.787)	<0.0001
Age	1.002 (0.996–1.008)	0.5477
Asian American subgroup		
Filipino American	1.000	
Vietnamese American	1.073 (0.915–1.259)	0.3869
Japanese American	0.947 (0.751–1.195)	0.6468
Chinese American	1.076 (0.854–1.356)	0.5339
Korean American	0.740 (0.549–0.997)	0.0480
Histology		
Adenocarcinoma	1.000	
BAC	0.874 (0.590–1.295)	0.5025
Squamous cell carcinoma	1.043 (0.870–1.250)	0.6497
Large cell carcinoma	1.302 (0.958–1.770)	0.0918
Undifferentiated/other/mixed	0.957 (0.803–1.140)	0.6195
Histologic grade[a]		
Well differentiated	1.000	
Moderately differentiated	1.262 (0.805–1.978)	0.3110
Poor differentiated	1.540 (1.003–2.363)	0.0482
Undifferentiated	1.470 (0.853–2.534)	0.1652
Period of diagnosis		
1991–1995	1.000	
1996–2000	0.890 (0.750–1.056)	0.1818
2001–2005	0.842 (0.701–1.013)	0.0678
Socioeconomic status	0.961 (0.910–1.015)	0.1539
Marital status[a]		0.4159
Married	1.000	
Unmarried[b]	0.935 (0.795–1.100)	
Surgery		<0.0001
No	1.000	
Yes	0.342 (0.270–0.432)	
Radiation		0.8854
No	1.000	
Yes	0.990 (0.859–1.141)	
Chemotherapy[a]		<0.0001
No	1.000	
Yes	0.595 (0.511–0.692)	

[a] Unknown included in the Cox proportional hazards analysis but not shown.
[b] Unmarried = single, separated, divorced, and widowed.
[c] Others included in the Cox proportional hazards model analysis but not shown.
OS, overall survival; AJCC, American Joint Committee on Cancer; HR, hazard ratio; CI, confidence interval; BAC, bronchoalveolar carcinoma.

With the exception of Japanese American patients (48.1%), the other four Asian American subgroup of patients were predominately native (born in their respective countries). Filipino American and Vietnamese American patients made up 70% of Asian American patients in this study. Although lung cancer is the most common cancer and most common cancer cause of mortality in Philippines,[14] there is limited literature about lung cancer patients who were never smokers in Philippines. We found that the majority of Filipino American female NSCLC patients were never smokers, and this proportion had been relatively constant during the 15 years of study period. The epidemiologic profile of Filipino American patients in this report may reflect the profile of lung cancer patients in Philippines. Similarly, in Vietnam, lung cancer is the most common cancer in men,[15] but the epidemiologic profile and survival outcome of lung cancer patients is again not well described. We observed that Vietnamese American female NSCLC patients had the highest proportion of never smokers among the five Asian American female subgroups, and this proportion had been increasing consistently over time (Figure 2*C*). In particular, the trend was statistically significant for Vietnamese American female patients reaching 89.1% ($p_{trend} < 0.0001$) during the 2001–2005 period.

Although the median age of Asian American never smokers as a group was marginally younger than ever smokers ($p = 0.0507$), we did not find a statistically significant difference in the median age of never smokers when compared with ever smokers among individual Asian American subgroups. This is likely as a result of the limited number of patients included in the study.

Similar to our previous report (Figure 4),[10] we did not find statistically significant OS differences between Asian never smoker and ever smokers as a group or among individual Asia American subgroups. This is likely a result of the limited number of patients in this study as larger studies have confirmed smoking status as an adverse prognostic factor for survival in NSCLC.[16] In addition, although stage 4 patients who did not receive chemotherapy had a median OS of 3 months regardless of smoking status, stage 4 patients who were ever smokers had a 5 months improvement in OS whereas never smokers had a 8 months improvement in OS when they received chemotherapy, in agreement with other retrospective analysis.[17] Prospective phase III first-line[5,6] and second-line[7] randomized trials of chemotherapy treatment in advanced NSCLC have also shown that never smokers had better median OS than ever smokers. For example, the recently presented Iressa Pan-Asia Study trial, which enrolled Asian never smokers in first-line treatment of NSCLC, reported a median survival of 17 months for never smokers who received carboplatin and paclitaxel combination chemotherapy, which is much higher than historical median OS for NSCLC patients (the majority were ever smokers) in first-line treatment trials.[6] This is likely as a result of combination of fewer genetic alterations and/or activation of a specific signaling pathway in the tumors of never smokers[2,18] and fewer comorbidities and better performance status in never smokers (Kawaguchi T, et al., submitted for publication). Never smok-

ers had a high proportion of EGFR mutations that generally carries a better prognosis.[19,20] Given that the majority of and significantly more never smokers with NSCLC presented with stage 4 disease and the better prognosis of these patients, it is imperative that these patients to be offered treatment.

The Cox proportional hazards analysis identified tumor-related factor (stage of diagnosis and histologic differentiation) and treatment-related factors (chemotherapy and surgery) as independent prognostic factors for OS. The nonsignificance of other well-known prognostic factors such as age, gender, and smoking status by multivariate analysis was likely as a result of low statistical power from the limited sample size. Although Korean American ethnicity was found to be a marginally significant favorable prognostic factor when compared with Filipino American, currently there is no biologic basis to account for this observation. In addition, given the limited number of patients and in particular Korean American patients in the Cox analysis in which other known prognostic factors are age and gender, we caution that this observation should be considered as hypothesis generating.

The major advantage of this study was our ability to abstract smoking status from a large population-based database as smoking status is not readily available from the CCR or the national SEER database. We were able to obtain smoking status without the need to link to other databases such as Medicare in which the analysis would be limited to a specific age group. The results from our method of abstracting smoking data from the regional registry is consistent with the prevalence of smoking data reported by the California Health Interview Survey, which showed within the general Asian American population Vietnamese women had the highest proportion of nonsmokers whereas Japanese women had the lowest proportion of nonsmokers.[21] In this study, Vietnamese female NSCLC patients had the highest proportion of never smokers (65.5%) whereas Japanese female NSCLC patients had the lowest proportion of never smokers (19.3%) (Table 2). Another advantage of this study was that we assigned AJCC stage to individual patients rather than assigning patients to the SEER summary staging system of local, regional, and distant disease. The use of the AJCC staging system provided a more accurate and relevant clinical synopsis of the patients especially such as initial stage at presentation and the benefits of chemotherapy in stage 4 patients.

The major limitation of the study was the limited patient size. As such, we did not observe statistical significant differences among individual Asian American subgroup according to smoking status. Another limitation of the study was that environmental tobacco smoke exposure was not recorded in the cancer registry. However, the genetic profile of never smoker regardless of second-hand exposure is different from ever smokers in terms of the frequency of EGFR and K-*ras* mutations[2] or the presence of *EML4-ALK* translocation.[18] Although most of the Asian American were born in their respective countries and this study may provide a synopsis of the clinicopathologic characteristics of never smokers with NSCLC especially Filipino Americans and Vietnamese Americans, we caution there may be "selection bias" as the Asian Americans that immigrated to the United States may be different than the general population in the native homeland and acculturation[22] since time from emigration. On the other hand, Japanese Americans were eventually split between native and nonnative. There seemed to be a trend that a higher proportion of never smokers among native compared to nonnative Japanese American patients. Although the number of Japanese American patients analyzed was certainly limited, the data suggest an environmental contribution to the etiology of never smokers. A comparison study with adequate sample size aimed at describing the difference in the clinicopathologic features between native and nonnative Asian American may provide more clues to the etiology of the high proportion of never smokers in Asia.

Our study represents the largest population-based analysis of NSCLC outcomes specifically related to Asian American subgroups while accounting for smoking status. However, in this analysis no major statistically significant clinicopathologic differences were observed among Asian American NSCLC subgroups. Our observational study was not designed to detect small differences across the various Asian American NSCLC subgroups, thus one cannot exclude the possibility of small differences because of limited sample size and power. For future clinical trial development, it is likely more appropriate to account for molecular tumor characteristics such as the presence of the EGFR mutations[6] rather than individual Asian American subgroup.

ACKNOWLEDGMENTS

The collection of cancer incidence data used in this study was supported by the California Department of Public Health as part of the statewide cancer reporting program mandated by California Health and Safety Code Section 103885; the National Cancer Institute's Surveillance, Epidemiology and End Results Program under contract N01-PC-35136 awarded to the Northern California Cancer Center, contract N01-PC-35139 awarded to the University of Southern California, and contract N01-PC-54404 awarded to the Public Health Institute; and the Centers for Disease Control and Prevention's National Program of Cancer Registries, under agreement 1U58DP00807-01 awarded to the Public Health Institute.

REFERENCES

1. Parkin DM, Bray FJ, Ferlay L, et al. Global cancer statistics. *CA Cancer J Clin* 2002;55:74–108.
2. Sun S, Schiller JH, Gazdar AF. Lung cancer in never smokers—a different disease. *Nat Rev Cancer* 2007;7:778–790.
3. Subramanian J, Govindan R. Lung cancer in never-smokers: a review. *J Clin Oncol* 2007;25:561–570.
4. Subramanian J, Govindan R. Molecular genetics of lung cancer in people who have never smoked. *Lancet Oncol* 2008;9:678–682.
5. Scagliotti GV, Parikh P, von Pawel J, et al. Phase III study comparing cisplatin plus gemcitabine with cisplatin plus pemetrexed in chemotherapy-naive patients with advanced-stage non-small-cell lung cancer. *J Clin Oncol* 2008;26:3543–3551.
6. Mok TS, Wu YL, Thongprasert S, et al. Gefitinib or carboplatin-paclitaxel in pulmonary adenocarcinoma. *N Engl J Med* 2009;361:947–957.
7. Kim ES, Hirsh V, Mok T, et al. Gefitinib versus docetaxel in previously treated non-small-cell lung cancer (INTEREST): a randomized phase III trial. *Lancet* 2008;372:1809–1818.
8. Miller BA, Chu KC, Hankey BF, et al. Cancer incidence and mortality

patterns among specific Asian and Pacific islander populations in the US. *Cancer Causes Control* 2008;19:227–256.
9. Kwong SL, Chen MS Jr, Snipes KP, et al. Asian subgroups and cancer incidence and mortality rates in California. *Cancer* 2005;104(12 Suppl): 2975–2981.
10. Ou S-HI, Ziogas A, Zell JA. Asian ethnicity is a favorable prognostic factor for overall survival in non-small cell lung cancer (NSCLC) and is independent of smoking status. *J Thorac Oncol* 2009;4:1083–1093.
11. Raz DJ, Gomez SL, Chang ET, et al. Epidemiology of non-small cell lung cancer in Asian Americans: incidence patterns among six subgroups by nativity. *J Thorac Oncol* 2008;3:1391–1397.
12. Ou S-HI, Zell JA, Ziogas A, et al. Low socioeconomic status is a poor prognostic factor for survival in stage I non-small-cell lung cancer and is independent of surgical treatment, race, and marital status. *Cancer.* 2008;112:2011–2020.
13. Zell JA, Ou S-HI, Ziogas A, et al. Epidemiology of bronchioloalveolar carcinoma: improvement in survival after release of the 1999 WHO classification of lung tumors. *J Clin Oncol* 2005;23:8396–8405.
14. Ngelangel CA, Wang EH. Cancer and the Philippine cancer control program. *Jpn J Clin Oncol* 2002;32(Suppl 1):S52–S61.
15. Le GM, Gomes Sl, Clarke CA, et al. Cancer incidence patterns among Vietnamese in the United States and Ha Noi, Vietnam. *Int J Cancer* 2002;102:412–417.
16. Florescu M, Hasan B, Seymour L, et al.; National Cancer Institute of Canada Clinical Trials Group. A clinical prognostic index for patients treated with erlotinib in National Cancer Institute of Canada clinical trials group study BR. 21. *J Thorac Oncol* 2008;3:590–598.
17. Tsao AS, Liu D, Lee JJ, et al. Smoking affects treatment outcome in patients with advanced nonsmall cell lung cancer. *Cancer* 2006;106: 2428–2436.
18. Wong DS-W, Leung EL-H, So KK-T, et al.; University of Hong Kong Lung Cancer Study Group. The ELM4-ALK fusion gene is involved in various histologic types of lung cancers from nonsmokers with wild-type EGFR and KRAS. *Cancer* 2009;115:1723–1733.
19. Calvo E, Baselga J. Ethnic differences in response to epidermal growth factor receptor tyrosine kinase inhibitors. *J Clin Oncol* 2006;24:2158–2163.
20. Sharma SV, Bell DW, Settleman J, et al. Epidermal growth factor receptor mutations in lung cancer. *Nat Rev Cancer* 2007;7:169–181.
21. McCracken M, Olsen M, Chen MS Jr, et al. Cancer incidence, mortality, and associated risk factors among Asian Americans of Chinese, Filipino, Vietnamese, Koreans, and Japanese ethnicities. *CA Cancer J Clin* 2007;57:190–205.
22. An N, Cochran SD, Mays VM, et al. Influence of American acculturation on cigarette smoking behaviors among Asian American subpopulations in California. *Nicotine Tob Res* 2008;10:579–587.